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## **LES SÉMINAIRES DE L'INMG**

*Understanding neuroblastoma biology  
through the analysis of its genetic and  
epigenetic landscapes*

Par

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**Mardi 30 janvier 2018**

**11 heures**

**Salle des Conférences**

**Médiathèque Paul Zech**

**Faculté de Médecine Lyon Est**

**8, Avenue Rockefeller**

**69008 LYON**

## Abstract :

Neuroblastoma is an embryonal neoplasm arising from the peripheral nervous system that accounts for 15% of cancer deaths in childhood. It is an enigmatic tumor presenting with a great genetic and clinical heterogeneity, both in terms of presentation and outcome.

The characterization of the genetic alterations observed in neuroblastoma led to the identification of major players of neuroblastoma oncogenesis that has considerably improved our understanding of the biology of this pediatric cancer. More recently, the analysis of the super-enhancer landscape allowed to decipher the core regulatory circuitries controlling the gene expression program of neuroblastoma. Distinct transcription factor networks predicate different tumor identities, corresponding to sympathetic noradrenergic or mesenchymal/neural-crest cell like identities. Cells of mesenchymal identity are more resistant to chemotherapeutic agents. Moreover, some neuroblastoma cells exhibit plasticity and are able to shift between the NCC-like and noradrenergic identities.

The understanding of cell identity, heterogeneity and plasticity in neuroblastoma has strong implications with respect to the development of new therapeutic strategies to eradicate tumor cells in neuroblastoma patients.

## Selected publications

- Boeva V *et al.* [Heterogeneity of neuroblastoma cell identity defined by transcriptional circuitries.](#) **Nat Genet.** (2017). 49:1408-1413.
- Lopez-Delisle L *et al.* Activated ALK signals through the ERK-ETV5-RET pathway to drive neuroblastoma oncogenesis. **Oncogene** (2017) *in press*.
- Eleveld TF *et al.* [Relapsed neuroblastomas show frequent RAS-MAPK pathway mutations.](#) **Nat Genet.** (2015) 47:864-71
- Cazes A *et al.* Activated Alk triggers prolonged neurogenesis and Ret upregulation providing a therapeutic target in ALK-mutated neuroblastoma. **Oncotarget** (2014) 5: 2688-2702.
- Cazes A *et al.* Characterization of rearrangements involving the ALK gene reveals a novel truncated form associated with tumor aggressiveness in neuroblastoma. **Cancer Res.** (2013) 73:195-204.
- Janoueix-Lerosey I *et al.* Somatic and germline activating mutations of the ALK kinase receptor in neuroblastoma. **Nature.** (2008) 455:967-970.